



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
[www.uspto.gov](http://www.uspto.gov)

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,039	04/25/2005	Holger Klapproth	Micronas.7837	9248
50811	7590	12/13/2007	EXAMINER	
O'SHEA, GETZ & KOSAKOWSKI, P.C.			SALMON, KATHERINE D	
1500 MAIN ST.			ART UNIT	PAPER NUMBER
SUITE 912			1634	
SPRINGFIELD, MA 01115			MAIL DATE	DELIVERY MODE
			12/13/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/520,039	KLAPPROTH ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	Katherine Salmon	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 21 September 2007.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 27-51 and 54 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 27-51 and 54 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date: _____   | 6) <input type="checkbox"/> Other: _____                          |

**DETAILED ACTION**

1. This action is in response to papers filed 9/21/2007. Currently claims 27-51 and 54 are pending. Claims 1-26 and 52-53 have been cancelled.
2. The following rejections for Claims 27-51 and 54 are reiterated. Response to Arguments follows.
3. This action is FINAL.

***Priority***

4. The English language translation of the foreign language document has been received.

***Withdrawn Objections/Rejections***

5. The objection to the specification made in section 4 of the previous office action is moot based on the amendments to the claims removing the phrase "at least microseconds".
6. The objection to Claims 30-31 made in section 5 of the previous office action is moot based on amendments to the claims to correct Markush language.
7. The rejections of the claims under 35 USC 112, second paragraph made in section 6 of the previous office action is moot based on amendments to the claims.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 27-29, 31-32, 34-37, 41-44, 46, 49-51, and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Kurane et al. (US Patent Application Publication 2001/0000148 A1 April 5, 2001).

With regard to Claim 27, Kurane et al. teaches immobilizing a probe on a solid support (preparing a carrier by immobilizing at least one receptor (e.g. a probe)) (p. 8 paragraph 161). Kurane et al. teaches forming a marker (fluorescent signal) and receptor (probe) complex (p. 8 paragraph 161). Kurane et al. teaches a processing step of analyzing the intensity of fluorescence emitted from the reaction system when the target is not hybridized to the probe (p. 7 paragraph 158), therefore, Kurane et al. teaches determining the number of receptors on the carrier by detecting the receptor-marker complex (i.e. the fluorescence emitted).

With regard to Claims 28-29, Kurane et al. teaches adding a target sample (ligand) and measuring the hybridization of the receptor (probe) and target (ligand) by measuring the fluoresce intensity (e.g. examining the test sample) (p. 7 paragraph 158).

With regard to Claim 31, Kurane et al. teaches the receptor is nucleic acid (abstract).

With regard to Claim 32, Kurane et al. teaches that reaction temperature can be varied so that it can be low enough to allow all receptor and ligands to bind or it can be increased such that there is no hybridization (the receptor and ligand are separate) (p. 9 paragraph 174).

With regard to Claim 34, Kurane et al. teaches a method wherein Figure 6 discloses two markers associated with 2 receptors (e.g. equal number of markers and receptors).

With regard to Claims 35-37, Kurane et al. teaches that the marker can be a fluorescent dye such as rhodamine and tetramethylrhodamine (a reactive group) (p. 6 paragraph 144).

With regard to Claim 41, Kurane et al. teaches that FRET can be used (p. 10 paragraph 190).

With regard to Claim 42, Kurane et al. teaches that the binding of the ligand to the probe (receptor) reduces fluorescence therefore the interaction of the ligand modifies FRET (abstract).

With regard to Claim 43-44 and 46, Kurane et al. teaches that a probe labeled with a fluorescent dye quenches when a target is hybridized (p. 2 paragraph 19). Therefore the receptor contains a dye which acts as a donor and the is quenched by an acceptor. Further, Kurane et al. teaches that hybridization of the ligand brings the donor and the acceptor of FRET into contact because Kurane et al. teaches that the hybridization of the ligand to the receptor decreases fluorescence.

With regard to Claim 49, Kurane et al. teaches immobilizing a probe on a solid support (preparing a carrier by immobilizing at least one receptor (e.g. a probe)) (p. 8 paragraph 161). Kurane et al. teaches forming a marker (fluorescent signal) and receptor (probe) complex (p. 8 paragraph 161). Kurane et al. teaches a processing step of analyzing the intensity of fluorescence emitted from the reaction system when the target is not hybridized to the probe (p. 7 paragraph 158), therefore, Kurane et al. teaches determining the number of receptors on the carrier by detecting the receptor-marker complex (i.e. the fluorescence emitted). Kurane et al. teaches that the marker can be a fluorescent dye such as tetramethylrhodamine (a reactive group) (p. 6 paragraph 144).

With regard to Claim 50, Kurane et al. teaches immobilizing a probe on a solid support (preparing a carrier by immobilizing at least one receptor (e.g. a probe)) (p. 8 paragraph 161). Kurane et al. teaches forming a marker (fluorescent signal) and receptor (probe) complex (p. 8 paragraph 161). Kurane et al. teaches a processing step of analyzing the intensity of fluorescence emitted from the reaction system when the target is not hybridized to the probe (p. 7 paragraph 158), therefore, Kurane et al. teaches determining the number of receptors on the carrier by detecting the receptor-marker complex (i.e. the fluorescence emitted).

With regard to Claim 51, Kurane et al. teaches coating the carrier with a polylysine prior to binding a receptor (preparing the carrier) (p. 8 paragraph 162).

With regard to Claim 54, Kurane et al. teaches adding a target sample (ligand) and measuring the hybridization of the receptor (probe) and target (ligand) by

measuring the fluoresce intensity (detecting receptor-ligand complexes) (p. 7 paragraph 158).

### **Response to Arguments**

The reply traverses the rejection. The reply asserts that the independent claims have a limitation of labeling the receptor after immobilization onto the carrier (Claims 27, 49, 50) (p. 12-14). The reply asserts that Kurane et al. does not teach this limitation but rather Kurane et al. teaches that the probe is preferably immobilized before immobilization to a solid support (p. 12-14 especially p. 12 2nd paragraph).

This argument has been fully considered but has not been found persuasive.

Though the preferred embodiment of Kurane et al. is to label the probe before immobilization, Kurane et al. does teach a method of labeling after immobilization. Kurane et al. teaches a nucleic acid probe not modified with a fluorescent dye is bound or fixed (e.g. immobilized) onto a surface of a solid support (e.g. a carrier). Kurane et al. teaches that before hybridization to the target nucleic acid (e.g. the ligand) is labeled with the fluorescent dye (e.g. label) (p. 8 paragraph 168). Therefore Kurane et al. teaches the limitation of adding the marker to the receptor after immobilization of the receptor onto the carrier.

9. Claims 33 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by Kurane et al. (US Patent Application Publication US 2011/0000148 A1 April 5, 2001) as applied to Claims 27-29, 31-32, 33-37, 41-44, 46, 49-52, and 54 and as evidence by Cremer et al. (US Patent 5922543 July 13, 1999).

Kurane et al. teaches immobilizing a probe on a solid support (preparing a carrier by immobilizing at least one receptor (e.g. a probe)) (p. 8 paragraph 161). Kurane et al. teaches forming a marker (fluorescent signal) and receptor (probe) complex (p. 8 paragraph 161). Kurane et al. teaches a processing step of analyzing the intensity of fluorescence emitted from the reaction system when the target is not hybridized to the probe (p. 7 paragraph 158), therefore, Kurane et al. teaches determining the number of receptors on the carrier by detecting the receptor-marker complex (i.e. the fluorescence emitted).

With regard to Claim 40, Kurane et al. teaches that the marker can be a fluorescent dye such as rhodamine and tetramethylrhodamine (a reactive group) (p. 6 paragraph 144). Cremer et al. teaches the half-life of rhodamine derivatives in the nanosecond range (Column 20 lines 4-6).

### **Response to Arguments**

The reply traverses the rejection. The reply asserts that the independent claims are not anticipated by Kurane et al. because Kurane et al. does not teach labeling the receptors after immobilization. However, as presented in the response to arguments above Kurane et al. teaches a nucleic acid probe not modified with a fluorescent dye is bound or fixed (e.g. immobilized) onto a surface of a solid support (e.g. a carrier). Kurane et al. teaches that before hybridization to the target nucleic acid (e.g. the ligand) is labeled with the fluorescent dye (e.g. label) (p. 8 paragraph 168). Therefore Kurane et al. teaches the limitation of adding the marker to the receptor after immobilization of the receptor onto the carrier.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kurane et al. (US Patent Application Publication US 2011/0000148 A1 April 5, 2001) in view of Sosnowski et al. (US Patent 6051380 April 18, 2000).

Kurane et al. teaches immobilizing a probe on a solid support (preparing a carrier by immobilizing at least one receptor (e.g. a probe)) (p. 8 paragraph 161). Kurane et al. teaches forming a marker (fluorescent signal) and receptor (probe) complex (p. 8 paragraph 161). Kurane et al. teaches a processing step of analyzing the intensity of fluorescence emitted from the reaction system when the target is not hybridized to the probe (p. 7 paragraph 158), therefore, Kurane et al. teaches determining the number of receptors on the carrier by detecting the receptor-marker complex (i.e. the fluorescence emitted).

However, Kurane et al. does not teach a carrier comprises of silicon, semimetal oxides, including SiO, and aluminum oxide.

Sosnowski et al. teaches the use of a carrier which is comprised of silicon (Column 9 lines 4-5).

Therefore it would have been prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Kurane et al. to use a silicon based carrier as taught by Sosnowski et al. The ordinary artisan would have been motivated to modify the method of Kurane et al. to use a silicon based carrier as taught by Sosnowski et al. because Sosnowksi et al. teaches that silicon layer provides a better chemical interface to provide a more stabile and robust carrier (Column 48 lines 20-28). The ordinary artisan would be motivated to produce a

carrier, which is stable and robust in order to produce a fabricated carrier comprising receptors, which could be used and stored easily without degradation.

### **Response to Arguments**

The reply traverses the rejection. The reply asserts that the independent claims are not anticipated by Kurane et al. because Kurane et al. does not teach labeling the receptors after immobilization. However, as presented in the response to arguments above Kurane et al. teaches a nucleic acid probe not modified with a fluorescent dye is bound or fixed (e.g. immobilized) onto a surface of a solid support (e.g. a carrier).

Kurane et al. teaches that before hybridization to the target nucleic acid (e.g. the ligand) is labeled with the fluorescent dye (e.g. label) (p. 8 paragraph 168). Therefore Kurane et al. teaches the limitation of adding the marker to the receptor after immobilization of the receptor onto the carrier.

12. Claims 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kurane et al. (US Patent Application Publication US 2011/0000148 A1 April 5, 2001) in view of Laugharn, Jr. et al. (US Patent 6245506 June 12, 2001).

Kurane et al. teaches immobilizing a probe on a solid support (preparing a carrier by immobilizing at least one receptor (e.g. a probe)) (p. 8 paragraph 161). Kurane et al. teaches forming a marker (fluorescent signal) and receptor (probe) complex (p. 8 paragraph 161). Kurane et al. teaches a processing step of analyzing the intensity

of fluorescence emitted from the reaction system when the target is not hybridized to the probe (p. 7 paragraph 158), therefore, Kurane et al. teaches determining the number of receptors on the carrier by detecting the receptor-marker complex (i.e. the fluorescence emitted).

However, Kurane et al. does not teach a marker comprising inherent fluorescence such as tryptophan.

With regard to Claims 38-39, Laugharn, Jr. et al. teaches a method using inherent fluorescence as labels (Column 13 lines 6-18). Laugharn Jr, et al. teaches that one of the labels can be tryptophan (Column 13 lines 6-18).

Therefore it would have been prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Kurane et al. to use a tryptophan label as taught by Laugharn Jr. et al. The ordinary artisan would have been motivated to modify the method of Kurane et al. to use a tryptophan label as taught by Laugharn Jr. et al., because Laugharn Jr. et al. teaches that labels such as tryptophan have a characteristic wavelength which can be detected without the need for separation of the product nucleotides from the substrate (Column 13 lines 6-18).

### **Response to Arguments**

The reply traverses the rejection. The reply asserts that the independent claims are not anticipated by Kurane et al. because Kurane et al. does not teach labeling the receptors after immobilization. However, as presented in the response to arguments above Kurane et al. teaches a nucleic acid probe not modified with a fluorescent dye is

bound or fixed (e.g. immobilized) onto a surface of a solid support (e.g. a carrier).

Kurane et al. teaches that before hybridization to the target nucleic acid (e.g. the ligand) is labeled with the fluorescent dye (e.g. label) (p. 8 paragraph 168). Therefore Kurane et al. teaches the limitation of adding the marker to the receptor after immobilization of the receptor onto the carrier.

13. Claims 48 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kurane et al. (US Patent Application Publication US 2011/0000148 A1 April 5, 2001) in view of Brenner et al. (US Patent 5695934 December 9, 1997)

Kurane et al. teaches immobilizing a probe on a solid support (preparing a carrier by immobilizing at least one receptor (e.g. a probe)) (p. 8 paragraph 161). Kurane et al. teaches forming a marker (fluorescent signal) and receptor (probe) complex (p. 8 paragraph 161). Kurane et al. teaches a processing step of analyzing the intensity of fluorescence emitted from the reaction system when the target is not hybridized to the probe (p. 7 paragraph 158), therefore, Kurane et al. teaches determining the number of receptors on the carrier by detecting the receptor-marker complex (i.e. the fluorescence emitted).

However, Kurane et al. does not teach a marker which is a microparticle.

With regard to Claims 48, Brenner et al. teaches microparticles used as fluorescent labels (Column 20 lines 30-45).

Therefore it would have been prime facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Kurane et al. to use a microparticle labels as taught by Brenner et al. The ordinary artisan would have been motivated to modify the method of Kurane et al. to use a microparticle label as taught by Brenner et al., because Brenner et al. teaches that microparticles permit resolution on a plane at a density between about ten thousand to one hundred thousand microparticles (column 20 lines 30-45). The ordinary artisan would be motivated to use microparticles in order to detect as many receptors as possible immobilized on the carrier.

### **Response to Arguments**

The reply traverses the rejection. The reply asserts that the independent claims are not anticipated by Kurane et al. because Kurane et al. does not teach labeling the receptors after immobilization. However, as presented in the response to arguments above Kurane et al. teaches a nucleic acid probe not modified with a fluorescent dye is bound or fixed (e.g. immobilized) onto a surface of a solid support (e.g. a carrier). Kurane et al. teaches that before hybridization to the target nucleic acid (e.g. the ligand) is labeled with the fluorescent dye (e.g. label) (p. 8 paragraph 168). Therefore Kurane et al. teaches the limitation of adding the marker to the receptor after immobilization of the receptor onto the carrier.

***Conclusion***

**14. THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katherine Salmon whose telephone number is (571) 272-3316. The examiner can normally be reached on Monday-Friday 8AM-430PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



Katherine Salmon  
Examiner  
Art Unit 1634

/Jehanne Sitton/  
Primary Examiner  
12/5/2007